Implications and limitations of cellular reprogramming for psychiatric drug development.

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Public Summary:
Human-induced pluripotent stem cells (hiPSCs) derived from somatic cells of patients have opened possibilities for in vitro modeling of the physiology of neural (and other) cells in psychiatric disease states. Issues in early stages of technology development include (1) establishing a library of cells from adequately phenotyped patients, (2) streamlining laborious, costly hiPSC derivation and characterization, (3) assessing whether mutations or other alterations introduced by reprogramming confound interpretation, (4) developing efficient differentiation strategies to relevant cell types, (5) identifying discernible cellular phenotypes meaningful for cyclic, stress induced or relapsing-remitting diseases, (6) converting phenotypes to screening assays suitable for genome-wide mechanistic studies or large collection compound testing and (7) controlling for variability in relation to disease specificity amidst low sample numbers. Coordination of material for reprogramming from patients well-characterized clinically, genetically and with neuroimaging are beginning, and initial studies have begun to identify cellular phenotypes. Finally, several psychiatric drugs have been found to alter reprogramming efficiency in vitro, suggesting further complexity in applying hiPSCs to psychiatric diseases or that some drugs influence neural differentiation moreso than generally recognized. Despite these challenges, studies utilizing hiPSCs may eventually serve to fill essential niches in the translational pipeline for the discovery of new therapeutics.

Scientific Abstract:
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